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EXAMINER	
KOSAR, ANDREW D	

ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
08/21/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/587,874	MATHIEU ET AL.	
	Examiner	Art Unit	
	ANDREW D. KOSAR	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-37* is/are pending in the application.

4a) Of the above claim(s) *29,30 and 33-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-28,31 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 November 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/16/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I and SEQ ID NO:1 in the reply filed on May 8, 2009 is acknowledged. The traversal is on the ground(s) that Applicant argues that taken as a whole, the invention "interpreted in light of the description" has unity. This is not found persuasive because the claims as drafted, embraced SEQ ID NO:1 and peptide fragments and "equivalent sequences" which are acknowledged by Applicant to be known in the art, and contrary to Applicant's assertion, the entire disclosure was considered in making the finding of a lack of unity. Furthermore, as discussed below, and identified in the international search report, peptides comprising SEQ ID NO:1, 2 and 3 are known in the art.

The requirement is still deemed proper and is therefore made FINAL.

Claims 29, 30, and 33-37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on May 8, 2009.

Claims 19-28, 31 and 32 have been examined on the merits.

Specification

Applicant's substitute specification filed November 16, 2006 is acknowledged.

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

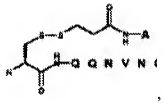
Claim Objections

Claims 20-25 and 32 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 19 is drawn to a peptide molecule, however the dependent claims are drawn to the peptide being further associated with a vector. The independent claim does not allow for 'further' modification beyond the addition of amino acids, as any additional elements, e.g. PEG, liposome, etc. are not within the boundaries of 'a peptide molecule'. Furthermore, the claims are not further limiting where the peptide vector is not directly attached to the peptide, as two peptides ionically bonded are not 'a peptide molecule'.

Claim 21 is objected to because of the following informalities: The claim recites 'a linear peptide comprising a domain of transduction of TAT protein of HIV-1 domains of transduction derived from the third helix of Antennapdia". 'Antennapedia' is misspelled. Additionally, it appears that there should be a comma between 'HIV-1' and 'domains'. Furthermore, "a domain of transduction" could be rewritten to conform with the English language to 'transduction domain', e.g. the transduction domain derived from the third domain of Antennapedia.

Claim 22 is objected to because of the following informalities: Claim 22 appears to be a literal translation of a foreign language document, and does not conform to standard English convention, and the statement after 'wherein' does not form a complete sentence. It is understood that each B is independently an amino acid with a basic side chain and each X is

independently an amino acid with an aliphatic or aromatic side chain, however the claim lacks such grammar.

Claim 25 is objected to because of the following informalities: While it is understood that the compounds shown are two peptides linked by a linker, e.g.  , the presence of the additional NH groups at the N-terminal of each peptide could lead to confusion in interpretation of the claims, as the N-terminal NH and C-terminal COOH are generally understood to be present, but generally not drawn. Furthermore, the linker cysteine N-terminus is missing the NH_2 group, being described only by N.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:
Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 19, 20, 23, 24, 26 and 31 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims are drawn generally to peptides comprising SEQ ID NO:1, 2 or 3, or an equivalent sequence. As shown in GOLDFARB (A.N. Goldfarb et al. J. Biol. Chem. (1998), 273(5), pages 2866-2873), peptides comprising at least 10 successive amino acids of SEQ ID NO:1 are naturally occurring, e.g. SCL (aka TAL-1) bHLH. SCL bHLH additionally comprises SEQ ID NOs: 1, 2 and 3. 'Equivalent' sequences are considered EP-2bHLH and MyoD bHLH.

Furthermore, these peptides are naturally expressed *in vivo* and *in vitro*, and thus are necessarily 'associated' with a vector to facilitate expression.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-24, 26-28 and 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Factors to be considered in making the determination as to whether one skilled in the art would recognize that the applicant was in possession of the claimed invention as a whole at the time of filing include: (a) Actual reduction to practice; (b) Disclosure of drawings or structural chemical formulas; (c) Sufficient relevant identifying characteristics such as: (i) Complete structure, (ii) Partial structure, (iii) Physical and/or chemical properties or (iv) Functional characteristics when coupled with a known or disclosed correlation between function and structure; (d) Method of making the claimed invention; (e) Level of skill and knowledge in the art and (f) Predictability in the art. While all of these factors are considered, a sufficient number for a *prima facie* case are discussed below.

Here, the claims are drawn to a peptide molecule that interferes with an HLH domain of TAL-1 comprising at least 10 successive amino acids from the HLH domain of TAL-1 (SEQ ID NO:1) or an equivalent sequence. Thus, the claims imply that any peptide comprising an epitope

of 10 amino acids or more of SEQ ID NO:1, or an equivalent sequence, would have such function.

The specification provides the full length SEQ ID NO:1 and two fragments of SCL bHLH (SEQ ID NOs: 2 and 3) and two conjugates of SEQ ID NO: 1 and SEQ ID NOs: 6 and 7 (through a linker). However, the specification fails to provide a sufficient number of examples within the genus of peptide and 'equivalents' claimed. The specification provides no description of contemplated equivalents, and provides no structure/function correlation for the plurality of peptides comprising at least 10 successive amino acids, to show which sequence(s) would function as claimed. Furthermore, the artisan understands that function cannot be determined from structure *a priori*, but must be determined *a posteriori*. Applicant has not described the requisite epitope to achieve the function, nor does the art recognize the epitope required to have the function claimed. Thus, while peptide synthesis may be a routine technique in the art, synthesis of peptides with the *a priori* knowledge that it will function as claimed is beyond the skill of the artisan.

Although the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond those compounds specifically disclosed in the examples in the specification. Moreover, the specification lacks a sufficient variety of species to reflect this variance in the genus. While having written description of SEQ ID NOs: 1-3, 6, 7 and the conjugates of compounds 4 and 5 (Table 1), the specification does not provide sufficient descriptive support for the myriad of compounds embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19-28, 31 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 19 and 31 recite 'or an equivalent sequence' and 'a sequence equivalent to the sequences.' It is unclear from the claims and specification as to what Applicant is considering 'equivalent'. Equivalence can be functional or structural, and functional equivalents may not be structurally related, and structural equivalents may not have the same function, thus it is unclear as to what Applicant is intending to claims. Additionally, with regards to claim 31, it is unclear what would be a sequence 'equivalent' to all three sequences.

Claim 20 recites 'associated with a vector', and it is unclear how a peptide is 'associated' with a vector. It is unclear whether is it merely proximity to a vector, or conjugated/bound to a vector, or whether the peptide functions as a vector.

Claim 21 recites the vector is selected from peptides, liposomes and PEG polymers, however claim 19 is drawn to 'a peptide molecule', and thus the vector cannot be PEG or liposomes.

Claim 22 recites "or a fragment thereof consisting of a sequence of at least 5 succesive amino acids of formulae (I) or (II)." It is unclear, as drafted, whether the vector is a fragment, or whether X is a fragment.

Claim 23 recites that the bond is selected from covalent, ionic, hydrophobic, cleavable or non-cleavable, however it is unclear what a 'hydrophobic bond' is, as it is not an art recognized bond type. Furthermore, all bonds are either cleavable or non-cleavable, and thus it is unclear how one distinguishes between ionic/covalent and cleavable/non-cleavable, when ionic/covalent bonds are inherently cleavable or non-cleavable.

Additionally, claim 23 lacks clear antecedent basis, as there is no support in the claim from which is depends for 'the physiological media' or 'the cells'.

Claim 24 recites that the bond may be direct or indirect, however it is unclear how a bond can be indirect, as a bond implies two things are connected. Interposing a linker between A and B is not 'a bond', regardless of the term 'indirect' being present. Furthermore, it is unclear to what the phrase 'and carried out by a functional group…' refers.

Claim 25 lacks clear antecedent basis, as the conjugate, with a non-amino acid (S-CH_2CH_2-C(O)) does not *per se* describe a peptide molecule, but a peptide conjugate.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 19, 20, 23, 24, 26-28, 31 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by GOLDFARB (A.N. Goldfarb et al. J. Biol. Chem. (1998), 273(5), pages 2866-2873, IDS 11/16/06).

Goldfarb teaches SCL bHLH (e.g. Figure 1, page 2868). The further portions of the peptide beyond SEQ ID NOs: 1, 2 or 3 can reasonably be considered 'a vector'. Additionally, E202 bHLH and MyoD bHLH are 'equivalents'. Having satisfied the structural requirements of the claims, the peptides necessarily must function as claimed. Goldfarb teaches that the sequences were expressed in yeast cells as fusions with a vector- LExA DNA-binding domain or B42 transcription activation domain (e.g. spanning pages 2867 and 2868). Further, Goldfarb teaches the peptides were placed in 10 mM sodium acetate, which is pharmaceutically acceptable a a vehicle for delivery, e.g. transdermal delivery.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 19-24, 26-28, 31 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goldfarb, above, in view of CALAS (AU 98/89889 B2, PTO-892 3/11/09).

The teachings of Goldfarb are presented above. Goldfarb does not teach the vector being derived from protegrin or tachyplesin.

Calas teaches the vectors $B(X)_2B(X)_4(B)_3(X)_6B$ and $B_2(X)_3B(X)_3B(X)_4(B)_2XB$, where X is an aliphatic or aromatic amino acid and B is a basic amino acid (e.g. claim 4) and specific examples of protegrins and tachyplesins (e.g. pages 4 and 5). It is noted that the vectors correspond to instant formulae (I) and (II), respectively. Calas teaches that the vectors are "new, non-toxic, system for vectoring active substances" into an organism (e.g. pages 6, 7a, 14, claim 7, etc.) and conjugated to an active substance (e.g. claim 8). Vectoring active substances into an organism necessarily requires the composition be pharmaceutically acceptable, and Calas teaches formulation as pharmaceutical compositions (e.g. page 16).

bHLH TAL-1 is a transcription factor, and thus it would be beneficial to vector it through a cell. It would have been obvious to have coupled the peptide of Goldfarb to the vector of Calas in order to vector the Tal-1 peptide into a cell, where Tal-1 will function as intended. One would have been motivated to have used the vector of Calas, as it is taught to be non-toxic and can deliver active agents across cell membranes without concomitant lysis of the cell. One would

reasonably expect the vector of Calas to deliver the peptide of Goldfarb into the cell where it will localize to the nucleus and activate transcription.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the foregoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Allowable Subject Matter

Claim 25 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph and claim objections, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

The following is a statement of reasons for the indication of allowable subject matter: The compounds of claim 25 comprise three elements: a delivery vector, a linker and a TAL-1 fragment, with each being individually taught in the art. However, the art does not teach or suggest the conjugate as claimed. One would note reasonably arrive at the claimed conjugates of claim 25 without the use of impermissible hindsight reconstruction.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANDREW D. KOSAR whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 08:00 - 16:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Andrew D Kosar/
Primary Examiner, Art Unit 1654